PATENT SPECIFICATION (11) 1 298 587

NO DRAWINGS

(21) Application No. 36413/70 (22) Filed 28 July 1970
(31) Convention Application Nos. 845 567 and 845 572
(32) Filed 28 July 1969
(31) Convention Application 1298 (32) Filed 7 Jan. 1970 in
(33) United States of America (US)
(45) Complete Specification published 6 Dec. 1972
(51) International Classification A61K 17/06 // C07C 169/02
(52) Index at acceptance
A5B 240 247 24Y 38Y 396
C2U 4A1 4C1 4C2 4C4 4C5 4X 6

(54) METHODS OF CONTRACEPTION AND CONTRACEPTIVE COMPOSITIONS

(71) We, AMERICAN HOME PRODUCTS CORPORATION, a corporation organised and existing under the laws of the State of Delaware, United States of America, of 685 Third Avenue, New York 17, New York, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to methods of contraception, to contraceptive compositions and to processes for making these compositions. More particularly it is concerned with methods employing and compositions containing 1-enantiomorphs of certain 13 - alkylgona-1,3,5(10) - trienes, which are useful for preventing conception or pregnancy in warm blooded, ovulating vertebrates.

It is a matter of common knowledge and experience to adminster orally oestrogens/progestogens in admixture or sequentially to ovulating vertebrates to prevent ovulation. The desired objective in nearly all instances, following daily administration of unit dosages of such well-known progestogens as norethindrone or norethynodrel and such well-known oestrogens as mestranol or ethynyloestnadiol, is to inhibit the production or release of gonadotropins from the pituitary and to suspend ovulation, thus preventing conception. In this manner, in live-bearing species, a luteoid endometrium is induced and maintained while the composition is taken for the inhibition of ovulation, that is, prevention of conception, and normal cyclic alterations may be induced.

Somewhat less well-known is a means to prevent conception by administration of a progestogen alone, on a daily basis, and often in very small amounts (the so-called "micro doses"). The exact mode-of-action of such materials is not entirely understood, but contraception has been demonstrated at dose levels that do not appear to alter pituitary function and thus do not inhibit ovulation. It is currently believed that agents of this type are effective by preventing the liquefaction of cervical mucus that occurs at about the time of ovulation in primates. Failure of the mucus to change in the "normal" way results in prevention of sperm migration into the uterus (of live-bearing species) and a prevention of impregnation. In these circumstances, the sperm do not migrate through the endo-cervical canal. To use this latter method to prevent conception, it has up to now been essential to administer the progestogens on a daily basis and recent reports by workers in this field suggest that duration of cervical action of certain progestogens is even less than 24 hours. As a result of the necessity for daily dosage (pill)-administration, the patient-failure rate has been high for this approach to contraception and method-failure rate has also been relatively high (compared with conventional oral contraceptives, first above-mentioned), presumably as a result of the short duration of action. Normal sperm migration through the reproductive tract of mammals to the site of fertilisation depends in part upon the characteristics of the cervical mucus, which are produced by the action of oestrogens on the cervical glands. Anti-oestrogens modify the characteristics of the mucus and prevent migration of the spermatozoa. To date only progestational anti-oestrogens are so employed.

All the oestrogens used previously have been steroids of the natural configuration, and all the progestogens have been steroids of the natural configuration, or in some instances racemates in which the enantiomer of the natural configuration is the active ingredient. We have now surprisingly found that *l* - enantiomorphs of certain 13 - alkylgona - 1,3,5(10)-

[*Price 25p*]